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FIGURE 1A

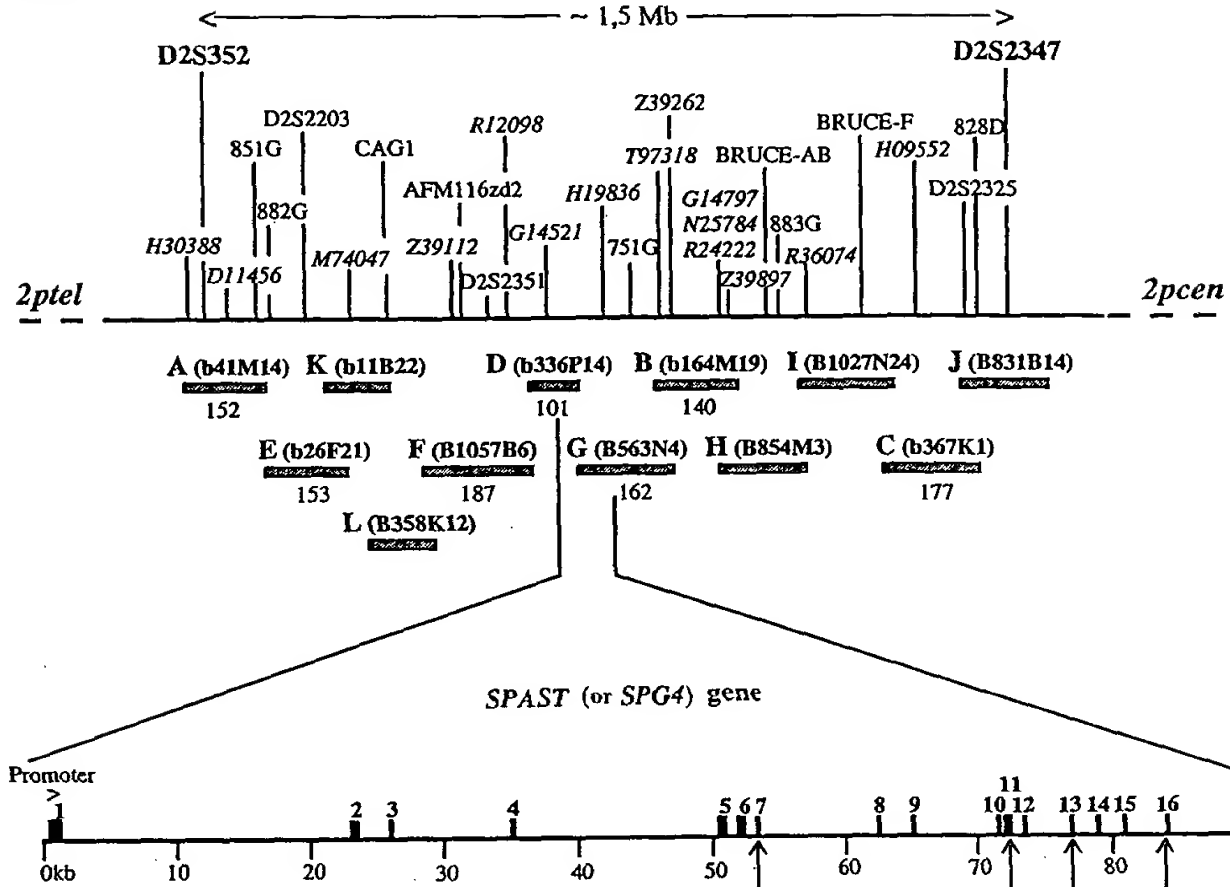
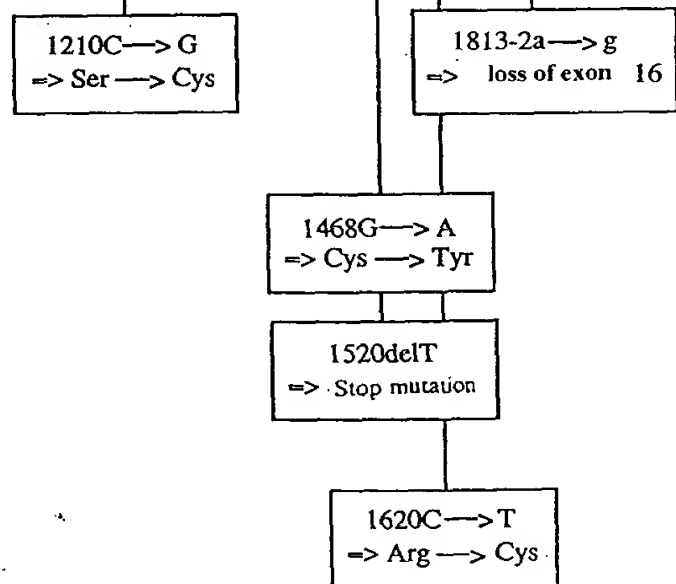


FIGURE 1B

FIGURE 1C



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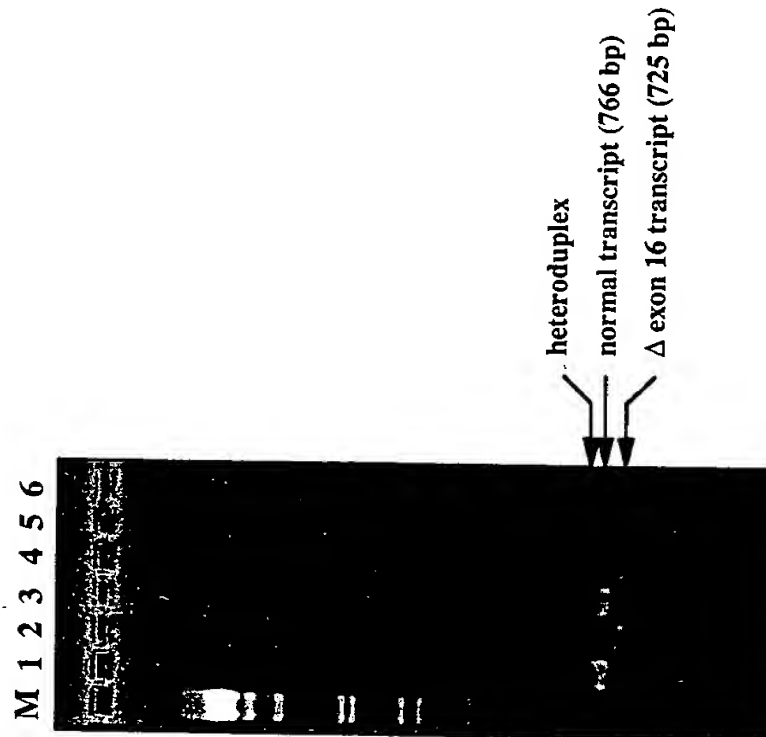
1 GCTCCTGAGACCGGCGGGCACACGGGGTCTGTGGCCCCCGCGTAGCAGTGGCTGCCGCGTTCGCTTGGTTCCCGTCCGGTCTGCGGGAGGCGGG 95
1 TTATGGCGGCGGCGGCGAGTGTGAATGAAATTCCTCGGGTGGACGAGGGAAGAAAGGCTCCGGCGGCGCCAGCAACCGGTGCCTCC 190
1 M N S P G G R G K K K G S G G A S N P V P P
CAGGCTCCGCCCCCTTGCCTGGCCCCCGCCCCCTCCGCGCGGGCGGCGCCCTCCGCGCGAGTCCGCGCATAAGCGGAACCTGTACTATTTCT 285
23 R P P P P C L A P A P P A A G P A P P P E S P H K R N L Y Y F S
CCTACCGCTGTGTTGAGGCTTCGCGCTGCTGCGTTTGGTTCGCTTCCACCTGGGGCTCTCTTCGTGTGGCTCTGCCAGCGCTTCTCCCGCGCC 380
55 Y P L F V G F A L L R L V A F H L G L L F V W L C Q R F S R A
CTCATGGCAGCAAGAGGAGCTCCGGGGCGCGCCAGCACCTGCCTCGGCGCTCCGCGCGGCGCGGTGCCGGCGGCGAGGCGGAGCGCGTCCG 475
86 L M A A K R S S G A A P A P A S A S A P A P V P G G E A E R V R
AGTCTTCCACAAACAGGCTTCGAGTACATCTCCATTGCCCTCGGCATCGATGAGGATGAGAAAGTGGACAGAAGGAGCAAGCTGTGGAATGGT 570
118 V F H K Q A F E Y I S I A L R I D E D E K A 2 G Q K E Q A V E W Y
ATAAGAAAGGTATTGAAGAACTGGAAAAAGGAATAGCTGTATAGTTACAGGACAAAGTGAACAGTGTGAAAGAGCTAGACGCTTCAAGCTAAA 665
150 K K G I E E L E K G I A V I V T G Q G 3 E Q C E R A R R L Q A K
ATGATGACTAATTTGGTTATGGCCAAAGGACCGCTTACAATCTTAGAAGATGCAACAGTTTTGCCATTTTCAAGTCACAAACGGACGCTA 760
181 M M T N L V M A K D R L Q L L E K M Q P V L P F S K S Q T D V Y
TAATGACAGTACTAACTTGGCATGCCCAATGGACATCTCCAGTCAGAAAGTGGAGCTGTTCCAAAAAGAAAAGACCCCTTAACACACACATAGTA 855
213 N D S T N L A C R N G H L Q S E 5 S G A V P K R K D P L T H T S N
ATTCACTGCCTCGTTCAAAAACAGTTATGAAAAGTGGATCTGCAGGCTTTCAGGCCACCATAGAGCAGCTAGTTACAGTGGTTTATCCATGGTT 950
245 S L P R S K T V M K T G S A G L S G H H R A P S Y S G L S M V
TCTGGAGTGAACAGGATCTGGTCTGCTCTTACCACCTATAAGTGTACTCCGAAAAAATAAGGACAAATAAACCCTTACCCCTACAACCTGC 1045
276 S G V K Q G S G P A P T T H K G 6 T P K T N R T N K P S T P T T A
TACTCGTAAGAAAAAGACTTGAAGAAATTTAGGAATGTGGACAGCAACCTTGCTAACCTTATAATGAATGAAATGTGGACAATGGAACAGCTG 1140
308 T R K K K D L K N F R N V D S N L A N L I M N E I V D N G 7 T A V
TTAAATTTGATGATATAGCTGGTCAAGACTTGGCAAAACAAGCATTGCAAGAAATGTTATTCTCTCTCTGAGGCGCTGATGTTTCAACAGG 1235
340 K F D D I A G Q D L A K Q A L Q E I V I L P S L R P E L 8 F T
CTTAGGCTCTCGCCAGAGGCTGTACTCTTTGGTCCACCTGGGAATGGGAAGCAATGCTGCTAAAGCAGTAGCTGCAGAAATCGAATGCAAC 1330
371 L R A P A R G L L L F G P P G N G K T M L A 9 K A V A A E S N A T
CTTCTTAATAATAAGTGTGCAAGTTAACTTCAAAATACCTGGGAGAGGAGAGAAATGGTGAGGGCTCTTTTGTGTGGCTCGAGAACCTC 1425
403 F F N I S A A S L T S K Y V 10 G E G E K L V R A L F A V A R E L Q
AACCTTCTAATTTTATAGTGAAGTTGATGCTTTTGTGTGAAAGAGAGAGGAGGAGACGATGCTAGTAGACGCTTAAACCTGAAATTT 1520
435 P S I I F I D 11 E V D S L L C E R R E G E H D A S R R L K T E F
CTAATAGAATTTGATGGTGTACAGTCTGCTGGAGATGACAGACTTGTGAATGGGTGCAACTAATAGGCCACAAGAGCTTGTATGAGGCTGTCT 1615
466 L I E F D G V 12 Q S A G D D R V L V M G A T N R P Q E L D E A V L
CAGGCGTTTCATCAACGGGTATATGTGCTTTACCAATGAGGAGCAAGACTACTTTTGTCTAAAAATCTGTTATGTAACAAGGAAGTCCAT 1710
498 R 13 R F Y V S L P S N E E 14 R L L K N L C K Q G S P L
TGACCCAAAAAGAACTAGCACAACTTGCTAGTATGACTGATGGATACTCAGGAAGTGACCTAACAGCTTTGGCAAAAGATGCAGCACTGGGTCT 1805
530 T Q K E L A Q L A R M 15 T D G Y S G S D L T A L A K D A A L G P
ATCCGAGTAACTAAAACAGAAACAGGTGAAGAAATATGTCTGCCAGTGAGTGAAGAAATATTCGATTATCTGACTTCACTGAATCCTTGAAAAAAT 1900
561 I R E 16 L K P E Q V K N M S A S E M 17 R N I R L S D F T E S L K K I
AAAACGAGCGCTCAGCCCTCAAACTTTAGAAGCTACATACGTTGGGAACAAGGACTTTGGAGATACCAGTGTAAAGGAAATACCTTTGTAAACC 1995
593 K R S V S P Q T L E A Y I R W N K D F G D T T V *
TGCAGAACATTTTACTTAAAGAGGAAACACAAGATCTTCAATGAACGTCATCGGCTACAGAAACAGCCTAAGTTTACAGGACTTTTTAGAGTCT 2090
TACATATTTGTGCACCAAACTTGAAGATGAACAGAAACAGACTTAAACAAAATATACAATGCAAAATGTAATTTTTGTGTGTTAAAGGCCTTGC 2185
CTTGATGGTCACAGTTATCCCAATGGACACTAAGTTAGAGCACAAACAACTGATTCTGGTCTCTTTACCAATATAATCATAATGTAAATAAT 2280
AATTTGTATATTTGTGTGCGATGAAAGTATTCAGGAACAGTGAATGGTAGAAGACACAAGAACATTGTTTGTGTTTCTTCTGATGTTTTTTC 2375
TTAAATAGTAATTTCTCTACTTTTCTTTCTACTGTTGTCTTAACTACAGGTGATTGGAATGCCAAACACTCTTAAGTTTATTTTCTTTTTC 2470
GTTTTATAAATTCAGTGTGCCAAATGAACTTTTTTCTAAGTAACTGTAATAGGAAAAAGTTTATTTTGAGAGTTTCTTCTCATAAATCTACA 2565
GACATTAACAAATTTGTGTGTTCTTTTACCTTTTATTTTCTATTACCTTGCTACCAAAACAGTTTAGATAGCAATATAATAGCAAAAAAGCAAA 2660
TATGGTAAAAATAGAGAAGTTTGAAGGTTTGAAGTTACTCTGTCTATATAACATGTAGATCAGTCTTCATGTGACCTGCAGTATTTTTTTCTAAT 2755
GTATTTGTGCAAAATCTGTTGTAGACTGTTAACTTCTTCTGATGGAATTTATTTTCTGCAAGAAATATTCTGATATTAAAGAGAGCCAAATTTA 2850
ACTGCTGTGAAATGTTTCCAGTGAAGAGAAGGAAATACTAGGAACCTAAGACATTTCTAATTTATTGCTTATTACTTTCTAATTTTACAGGA 2945
TAATTATAAGCAAGTGAACCTACCACTTTTATTCTTAATAATTATTAATCCCTTCAATGAACTTTAAAAAACTGAATTTTTATACATGGCAT 3040
ACATTTTCTAGTTCCTTCTGCTTGTCTTTATTAACCTCAAAAGTTCTAGTCTAGTCTGTTGATCTGCCTTTTGTCTCCCAAAATGTACAGTAAT 3135
TCCATTTGTTGTATAAATATGCCTGGATTTTCAATATAAAATGTCATTGTAGGGAGTAGAGACTCATATCATGGCCTTTTAAATATTGTAATA 3230
AAGGCAATAGATATTTGCCCTTAGTTACTGG 3263

FIGURE 2

09/830902

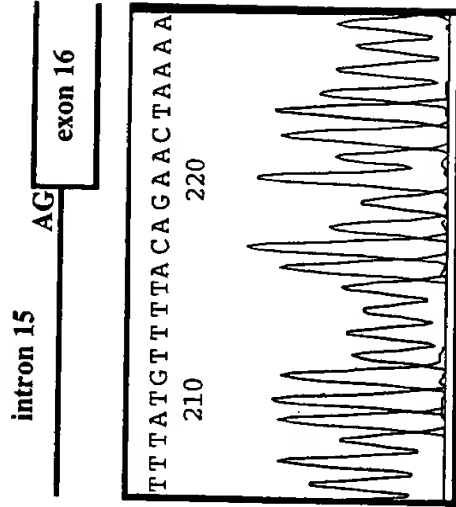
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A



B

Normal acceptor splice site



Mutated acceptor splice site

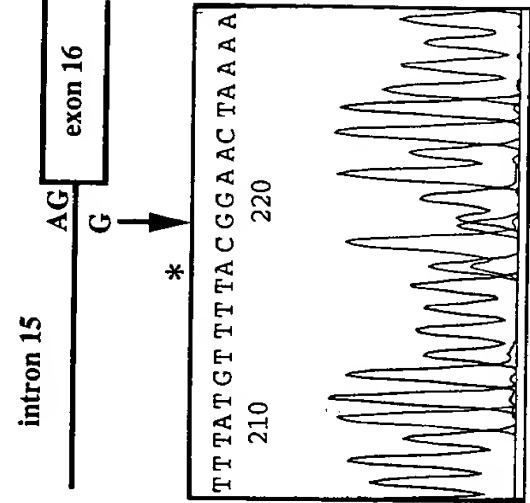


FIGURE 3

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TBF6_YEAST      -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
Q02845_YEAST    -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
SAP1_YEAST      MDSQRSHHILTLTKIERRPQOPLDTFTELYSRIANEZIIYYLNLEEKKRYKEALQGNKALTTDVLFRQTLIEHNYFTQSYTKDEVSLQNGIREL
SKD1_MOUSE      -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
EN13_YEAST      -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
SPAST_HUMAN     -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
SPAST_MOUSE     -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
O43078_SCHPO    -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
O16299_CAEL     -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI
Q18126_CAEL     -----MAHEKFS-----IPEN---FTLAQS---LQLLSGVKNQYKNLADLIINSKGNKDVTVYCK---IHKNLDTLLVYVH-----EGLRKI

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TBPF6_YEAST      -----
Q02845_YEAST     - E K T Y T L K K G L G N L V V D H P E L R S I E D ----- F Q I L - G Q D I R I A R R K A E T L M A E G N G S T S L S S S S S V L C L G T C N G L R F F K
SAFI_YEAST       Y H K S V M H L K R V K L V R E E P A P R N D M P S S K T Y I T N R S S S T T R E T E P F V F Q N V P G E M M K T L E R N H A C C Y K T A Y S H F S L S S Y G N S T S I K R G E D A E H I R
SKDI_MOUSE       -----
EN13_YEAST       -----
SPAST_HUMAN      -----
SPAST_MOUSE      -----
O43078_SCHEPO    -----
O16299_CAEEL     -----
Q19128_CAEEL     S A S N C N C V L K S H S K S V P V T I K V S T K L C A P A C Q Q S C S C Q Q D N Q T I A N N A D T N C I S Q C A R K C Q A R C G I Q N G M C F Q Q S P A T T T D A I P I V I R L E I T S G S

```

TBP6_YEAST
 Q02845_YEAST
 SAPI_YEAST
 SKDI_MOUSE
 EN13_YEAST
 SPAST_HUMAN
 SPAST_MOUSE
 Q43078_SCHPO
 Q16299_CAEL
 Q18128_CAEL

LWRMGSKRDKLKEADEKEAKINKQADNIRRAKLEEEKKLGAKLQYERDL--LQREKLIELKVKKEVEFEVAQKLE--EERVKREEE
 VNFVPSKPLSNNASRQKNPIEHNDPFLKKETELYSDKYISEPILIDLTROEDDDHVGILKGNVYDEESDGFEDVDSDYDNYSEVDDVEEEE
 --MNSPGCGCKKKKSGCCASNPFVPPPPPPCLAPAPPAAGPAPPFESPKRKNLY--YFSYPLFVGFALLRLVAFHGLLFLV-WLCQRFSSRALH
 LLCENGRDWACAYYSYCKVLEEMKKSSAANDRMGLPLTCAEACSWNGLYDNCLSKASKLRKTIIESEMERQHYQLAAKLSKKAPVDLHPLRFVR
 SINSQCAPKCIQCNHQCASQNKTNQCANECNHNQCANSCSPSTSSYSKCVSQCAETCCAGSNVTSNKQQCQQCQSQNTCCQGYQSTVSTTTTII

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TBPS_YEAST      Q02945_YEAST  ERKBR-----EQAEKKRISTLKHERKTN-YKSRASLDNFGSSSSKSSGKIDN-----SLIKRRSLDVRVTSGERVTP-----MEAAEYIC--
SAP1_YEAST      EKEERRRIKT--LEAIQQQMSDLVSTBSTSTSNKSVSSSENVPFGSCIQSLPTTAPALPSLFPFPLNLNVDRASSTGALKPNSLETSTHTDSSKIRNP
SKD1_MOUSE      EN13_YEAST    AAKRSS-----GAAPAPASASAPAPVPGGEAEVRVVFHKQAFEYIS-----IALRIDEDEKACQEQEAVEWKKKIEELEKC--
SPAST_HUMAN     SPAST_MOUSE  SQTAYTPTMT--TRMXYQTRGACQSEVNLSTPKQIYKSHKSPFSTSTAFVISSSYIC-----DAPSYLAPSKRNPFPPLKEDPTFASFHSSAGATAAA
O43078_SCHPO    ALARNGISPY--FTGKPRRKIVTETPDSDAQQQQPPFKRSRQONQLDLDELGLI1D--EDEDRTVDVDFBQKQDTRKLSRQVPLFGKSSQFKLCEI-
Q16299_CAEEL    Q19128_CAEEL QIVNLNVLNNGSSCEPCCQCNQCAQQQSQOQCAQCCQTCGVAQPFMTAFS-----KCPACSTSDYDRAVQKQGDYCEKKRRAAEMDELTKH

```

[illegible]

TBP6_YEAST IKSPITLNLQNSKSNISNIPITNSKLKASKSNTNKHVSRRNEQNLEPS--SPVLVLSAT--AVFAESK--PMRSKSGCTPDKESASSSSLDSRKE----
 O20445_YEAST IKSPITLNLQNSKSNISNIPITNSKLKASKSNTNKHVSRRNEQNLEPS--SPVLVLSAT--AVFAESK--PMRSKSGCTPDKESASSSSLDSRKE----
 CAP1_YEAST LKSKATKVPNSSSKKT--SNKSKASKSNTNKHVSRRNEQNLEPS--SPVLVLSAT--AVFAESK--PMRSKSGCTPDKESASSSSLDSRKE----
 NAD1_MOUSE E-EALQQLQHAVQYVLHVWVYEAQGDKAQKQISVIRGCTETLHRAAPLQKLLKLESL--KKPQK--VKGAQGGPVDEKGGSDSGSAESDD--
 EN13_YEAST E-EAYTAYTQVLDLMLLALKYE--KNPKSKDLIHAKETLHRAAPLQKLLKLESL--KKPQK--VKGAQGGPVDEKGGSDSGSAESDD--
 SPAST_HUMAN LQSESGAVFKKKDPLTNTSNALPKCTVMKTKSCAGLSCGSHBAPSLGSLMVSGVQCQSGPPTT--BKGTGKFNPRNTKISGTPPTAVRKKKD--
 SPAST_MOUSE LQSESGAVFKKKDPLTHASNLPRSKTVLTKGSGACSLGSHBAPSLGSLMVSGVQCQSGPPTT--BKGTGKFNPRNTKISGTPPTAVRKKKD--
 CA03078_SCEPO APIPLFVAVPVLTSASHSSSDGSKRHKPSTKYPLNLSHDTLCL--ASTRPSASDAGSPATSP--PATADSGITVKITSGISTTQQTFE--
 O16299_CAELP NPKRRAAIQNTGLTYSFTTAAAGQDQNSKTFQVPLRDSQSSQAGSLGICAPFPARR--APDIPKRNSEFLIRKAMGCHDTGGCGDKMGLR--
 O19128_CAELP PASAARVTPFRTTARAPEKKAARAKKENDRHVCSKRGCDASBQHVTKKSDTVHPPEKSDNSNRMETVTKRVYDKASLPHQNVVRA--

TSFP6_YEAST	-----DILKSQGVDBRNACEQILNEILVTDEKVIYWE	I	LRN	NS	K	A	V	I	FLR	DL	K	L	E	V	R	M	F	T	TLMIKA
Q02845_YEAST	-----DILKSQGVDBRNACCEQILNEILVTDEKVIYWE	I	LRN	NS	K	A	V	I	FLR	DL	K	L	E	V	R	M	F	T	TLMIKA
SAP1_YEAST	KKVLREILEDEIIPDLSQGVDBRQAQAKQITAEIVSVGDEVDND	I	LRN	NS	K	A	V	I	FLR	DL	K	L	E	V	R	M	F	T	TLMIKA
SKDI_MOUSE	-----PEKKKKLQOQCALVIERPNNVKWE	V	LEG	EA	K	A	I	L	SKF	EL	T	N	K	T	G	I	F	N	TLHARA
EN13_YEAST	-----CGEDNKKLRGALSAILSKPPNNVKWE	V	LEG	EA	K	A	I	L	SKF	EL	T	N	K	T	G	I	F	N	TLHARA
SPAST_HUMAN	LKNFRVDSNLANLNMNEIVDNGTAVKFD	I	QDL	OA	Q	I	L	IL	SKF	EL	T	N	K	T	G	I	F	N	TLHARA
SPAST_MOUSE	LKNFRVDSNLANLNMNEIVDNGTAVKFD	I	QDL	OA	Q	I	L	IL	SKF	EL	T	N	K	T	G	I	F	N	TLHARA
O43078_SCFPO	LQQTTPSSDFEYAMNNEIISNHEPVYIS	I	LDD	NS	K	A	I	Y	FLR	EL	Q	L	E	V	O	M	F	T	TLHARA
O16299_CAEL	AEPTLKHFDENITSLSEZSMVNNNEICWA	V	LEG	KA	E	I	VL	FKK	DL	T	I	A	P	K	V	I	F	N	TLICRC
Q18128_CAEL	ALLNGCVKDVIGERIKDELVDLND -TCGRMDV	V	CHS	AA	E	A	I	L	ALN	NL	K	L	O	V	I	F	N	TLILKA	

[illegible]

TBP6_YEAST	SSATAQSE--DRNHT--	LDSEV	LC	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
Q01845_YEAST	SSATAQSE--DRNHT--	LDSEV	LC	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
SAP1_YEAST	SSAAACSNKSNTHNSDTNGDEDDT	TV	LA	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
SKD1_MOUSE	GVNDNG--	I	LC	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
EN13_YEAST	CNDGQC--	I	LC	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
SPFAST_HUMAN	QSGADD--	RV	MG	R	QSEL	E	VAR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
SPFAST_MOUSE	QSGADD--	RV	MG	R	QSEL	E	VAR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
O43078_SCHPO	TNAAPFKQTC--	HSRPF	LA	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
Q16299_CAEL	NTAPDE--	RL	LC	L	WAL	D	AR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS
Q18128_CAEL	TSSADD--	RI	IG	R	QSEL	E	VAR	SEKKLYIP	DYET	LYHLKRLMAKQ--	KNGLQDLDELITEM	E	F	GS

[illegible]

```

TBP6_YEAST      -----
Q02845_YEAST    EWSSKFGSNGS-----
SAP1_YEAST      KWASQFGSNGS-----
SKD1_MOUSE      KFTEDFGQEG-----
ENL3_YEAST      QFTEDFGQEG-----
SPAST_HUMAN      RWNKDFGCDTIV-----
SPAST_MOUSE      RWNKDFGCDTIV-----
O43078_SCHPO    EWNKQFGSQR-----
Q16299_CAEEL    AWDKKFGCLFPFSSR-----
O18128_CAEEL    DFRSFG-----

```

FIGURE 4A

[illegible]

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AFG3_YEAST ---MMHWQRYARGAPR-----SLTSL-----FGKASRISTVKP-----VLSRMPVBRQLQTLGLSLATR-----NTIHR--S
RCAL_YEAST ---MLLSWSRIATKVVRRPVFRSYGLTHIKSLHTQYRLNRLQENKSGNKNEDNEDAKLNKEIPTDEEVEAIRKQVEKYIEQTKNNTIPANWK
PARAPLEGIN MAVLLLLLRALRRGPGGPR-----PLNGPGPAWS-PCFPARPGCRP-----YMASRPPGD--LAEAGGRALQ-----S
YME1_YEAST ---MNVSKILVSPVTN-----VLRIFAPRLPQIGASLLVQKKWA-----LRSKKFYRFYSEKNSGEMPP-----K
SPAST_HUMAN ---MNSPGCRGKKKSGCASN-----PVFPRPPPCAPAPPAAGPAPP-----ESPHKRNLYFYSPLFVGFFALLRLVAFHGLGLLVWLC

AFG3_YEAST TQIRSFHISWTRLN-----ENRPNKE---GEGKNNGKNADNNSNKEDGDKRNEFGSL-----EYFRSKEFANTMFLTIGFTIIF
RCAL_YEAST EQKRRKIDESIRRLLEDVVKQESNRIOEERKEKEENGFSKAKSNRKEGGYFEGNNSRNIPPPPPPPKPLNDPSNPVSKNVNLFQIGLTFLL
PARAPLEGIN LQRLRLTPTTFEGINGLLKQH---LVQNPRVRLWQLGGTYFYNTSRLKQKXKXKSKGKAPEDDE---EERRRRERDDQMYRERLRTLLV
YME1_YEAST KEADSSGKASNKST-----ISSIDNSQP---PPPSNTNDKTKQANVAVSHAMLATREQEA-----NKDLTSFDAQAIFYKLLQSNY
SPAST_HUMAN QRSRALMAAKRSSGAAPAP---ASASAPAPVP---GGEAEVRVVFHQAFAEYISALRLDEDEKAG-----QKEQAVEWYKKGIEELEKGIIV

AFG3_YEAST TLLTPSSNNSGDDSNRVLTFQDFKTKYLEKGLVSKIYV---NKF-LVEAELVN-----TKQVVSFTIGSV---DIFEEQ---MDQIQDILLNI
RCAL_YEAST LSFLLDLLNSLEEQS-EITWQDFREKLLAKGYVAKLIV---NKS-MVKVMLNDNGKNQADNYGRNFYVFTIGSI---DSFEH---LQKAQDELDI
PARAPLEGIN IAVVMSLLNALSTSGGSIWNDFVHEMLAKGEVQVRQV---ESDVVEVYLHPGAVVFCRPRALMYRNQVANI---DKFEK---LRAAEDELNI
YME1_YEAST PQYVVSRTFETFGIASSPECMELVMEALQIRGRSEADA---RON-LLTASSAG-----AVNPSLASSSSNQ---SGTRGN---FESMYSPLYG
SPAST_HUMAN IVTGQGEQCERARRLQAKMNTNLVMAKDRQLQLEKMQP---LFFSKSQTDVYNDSTN---LACRNGHLSQESGAVPKRKDPLTHTSNLSFRSKTVMKT

AFG3_YEAST PPRDRIPIKYIERSSPFTFLPFF---LPTIILLGCLYFTRKINSPPNANGGGGGGLGGMFNVGKSRAKLFNKETDIK---IS---KNVA---CDE
RCAL_YEAST DKDFRIPVLYVQEGNMAKAMFOI---LPTVIMAGIIMLTRES-----AQAGGSRGGIFGLSRKAKKFNFTETDVK---IK---KDVV---CDE
PARAPLEGIN EAKDRIPVSYKRTGFFGNALYSV---GHTAVGLALWVYFRLAG-----MTGEGGSAFHLQKMARFTIVDGKMGK---VS---KDVV---CDE
YME1_YEAST SRKE---PLHVVSSESTFTVSRW---VKWLVFGLITYSFSEG-----FKYITENTILLKSSEVADKSVDAKTN---VK---DDVC---CDE
SPAST_HUMAN GSAGLSGHRAPSYSGLSMVSGVKGSGPAPTHKGTPTNRNKNKSTPTTATRKKKDLKNFRNVDNLANLIMNEIVDNGTAVK---DDIA---QDL

AFG3_YEAST KQEIM---BFLKH---GKYTKLGAKIPR---AI---S---T---L---K---T---G---ANVP---LSVSGSEFVEMFV---ASRV---D---TQ---SMA---S---IF---I
RCAL_YEAST KEEIM---SFLKE---SRYEKMGAKIPR---AI---S---T---L---K---T---G---AGVP---YFVSGSEFVEMFV---ASRV---D---TQ---SMA---S---IF---I
PARAPLEGIN KLEVR---DYLLK---ERFLOLGAKVPR---AL---L---C---L---K---V---T---G---AGVP---LAMAGPEFVEVIG---LAARV---S---KE---SARA---C---VY---I
YME1_YEAST RAELE---DPLKD---TKYESLGGKLPK---VL---T---L---L---K---T---G---AGVD---FMSGSEFDEVYV---AKRI---D---AQ---SRA---A---IF---I
SPAST_HUMAN KQALO---ILPSLR---ELFTGLRAPA---R---LL---F---N---M---K---V---A---SNAT---FNISAASLTSKYV---EKLVA---A---AV---ELQ---S---IF---I

AFG3_YEAST AIGKE---GKGGALGGANDEREATLNQL---V---M---T---T---S---DQVVVLG---RPDV---N---LM---PG---FDRHIQIDS---DVNG---QOIYLVHLKRLNLDPLLT
RCAL_YEAST AIGKA---QKG---NFGSANDERENTLNQM---V---M---T---T---S---DQVVVLG---RPDI---N---LL---PG---FDRHINIDK---ELEG---KAIFAVALHLKLAGEIF
PARAPLEGIN AVGKK---STT---MSGFSNTEEEQTLNQL---V---M---T---M---G---T---D---DVIVLAS---RADI---G---LM---PG---LDRHVFIIDL---TLQE---REIFEQHLKSLKLTQSST
YME1_YEAST AIGGK---NPK---DOAYAKQTLNQL---V---L---L---F---S---Q---T---SGIIIGAT---FPEA---N---LT---PG---FDKVVNVDL---DVNG---ADILKHHMKKITLADNDV
SPAST_HUMAN SLLCE---REG---EHDSARRLKTEF---I---F---V---Q---S---A---G---D---D---R---V---L---V---N---G---A---R---P---Q---E---E---V---L---FIKRVYVSI---NEET---LLLLKNLLCQGSPLTQK

AFG3_YEAST DDMNLSGKL---TL---P---T---T---ADIANACNE---LIAARNDPYITIHFEQ---IERVIAGLEKKTRV---SKEEKRSVAYHEAGE---VCGWFLKYADPLLV
RCAL_YEAST DLKN---RL---AL---P---FS---ADIANVCNE---LIAARSDDEDAVKLNHFEQ---IERVIGGVERSKSL---SPEEKVVAYHEAGE---VCGWFLKYADPLLV
PARAPLEGIN FYSQ---RL---EL---P---FS---ADIANICNE---LBAAREGTSVHTLNFEV---VERVLGATAKSKSL---SKEEQKVAFHEGSE---LVGWMLHTEAVMKV
YME1_YEAST PTII---RL---P---L---S---AELANLVNQ---VYACQKNAVSVDMSHFEV---KDKILMGAERKTMV---TDAARKATAFEAGE---IMAKYTNATGATLYKA
SPAST_HUMAN ELAQ---L---RM---D---YS---SDLTALAKD---LGPIRELKPQVKN---MS---SEMRNIRLSDFTES---KKIKR---SVSPQTLKE---YIRWNKDFGDTTV--

AFG3_YEAST SIIPRGQCALGYAQLPDDQYLISEEQFHRHMIMALGGRVSEELHFP---SVTSGAHDFFKKVTOMANAMVTSLGMSPKIGYLSFDQNDG---NFKV
RCAL_YEAST SIIPRGQCALGYAQLPDDQYLISEEQFHRHMIMALGGRVSEELHFP---SVTSGAHDFFKKVTOMANAMVTSLGMSPKIGYLSFDQNDG---NFKV
PARAPLEGIN SITPRNAALGFAQMLPRDQHLFTKEQLFERMCMALGGEASEALSFN---EVTSGAQDDLEKVTIRIAYSMVQKFGMAFGICGISFPEAQEGLMGIG
YME1_YEAST TILPRGRALGITFQLPEMDKVDITKRECOARLDVCMGGKIAEELIYKDNNTSGCGSDLSQATGTARAMVTVQYGMSSDDVGPVRLSENW-----
SPAST_HUMAN

AFG3_YEAST NKPFNSKTARTIDLEVKSIVDDAHRACTELLTNLPRVDLVAKELLRKEAITREDMIRLLGPRP-FKERNEAFEKYLD-----PKSNTPE
RCAL_YEAST TKPFSDETGDIIDSEVYRIVQECHDRCTKLLEKAEDVEKIAQVLLKKEVLTREDMIDLLGKRP-FFERNDADFYLNDYETEKIRKEEEKNEKR
PARAPLEGIN RRPFSQGLQOMMDHEARLLVAKAYRHTKEVLQDNLDKLQALANALLEKEVINYEDI EALIGPPPHGPKKMIAPQRWIDAQR-EKQDLGEEETEET
YME1_YEAST -ESWSNKIRDIADNEVIELLKDSEERARLLTKKNKGRVLLVQGLIYETLDAHEIEQVCKGEK-LDKLKTSTNVTNVVEGPD--S-DERKDIGDDK
SPAST_HUMAN

AFG3_YEAST PEAPAAATN-----
RCAL_YEAST NEFKPSTN-----
PARAPLEGIN QQPPLGGEEPTWPK
YME1_YEAST PKIPTMLNA-----
SPAST_HUMAN

FIGURE 4B

FIGURE 5

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FIGURE 6.B

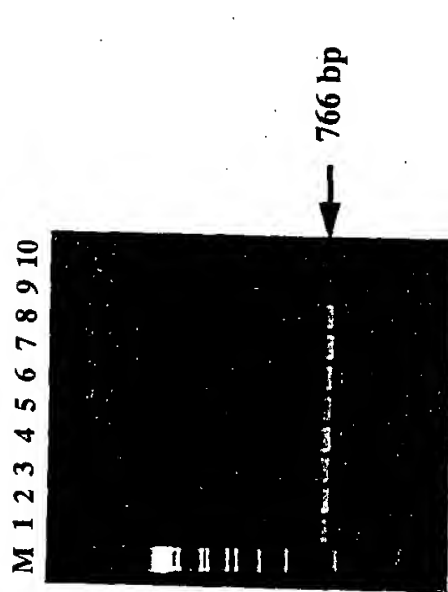


FIGURE 6 C

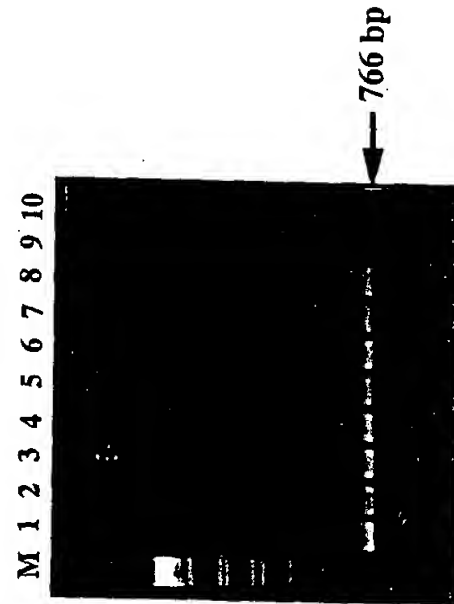


FIGURE 6 A

